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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,186	06/29/2001	Joshua Levin	PB/5-31481A	9567
22847	7590	08/05/2004	EXAMINER MEHTA, ASHWIN D	
SYNGENTA BIOTECHNOLOGY, INC. PATENT DEPARTMENT 3054 CORNWALLIS ROAD P.O. BOX 12257 RESEARCH TRIANGLE PARK, NC 27709-2257			ART UNIT 1638	PAPER NUMBER

DATE MAILED: 08/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

944

Office Action Summary

Application No.

09/896,186

Applicant(s)

LEVIN ET AL.

Examiner

Ashwin Mehta

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 7/21/2004 & 5/21/2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25-28,38,39,44,47,51-54,58 and 59 is/are pending in the application.
- 4a) Of the above claim(s) 51 and 52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25-28,38,39,44,47,53,54,58 and 59 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 June 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>5232003</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The Examiner was not aware of Applicants' supplemental amendment filed July 21, 2004 before issuing the Notice of Non-Responsive Amendment mailed July 26, 2004. The aforementioned amendment is responsive to the Office action mailed January 21, 2003, and the Notice of Non-Responsive Amendment mailed July 26, 2004 is hereby VACATED.
2. The objections to claims 58 and 59 are withdrawn in light of the claim amendments.
3. The rejection of claims 25-29, 38, 39, 58, and 59 under 35 U.S.C. 101 is withdrawn in light of the claim amendments.
4. The rejections of claims 25-29, 38, 39, 43, 45, 46, 51, 52, 58, and 59 under 35 U.S.C. 112, 2nd paragraph, are withdrawn in light of the claim amendments or cancellations.
5. The rejection of claims 25, 29, and 59 under 35 U.S.C. 102(b) is withdrawn in light of the claim amendments or cancellation.

Election/Restrictions

6. Claims 51 and 52, as amended, are directed to non-elected inventions and claims 44, 47, and 53 still contain non-elected subject matter that must be deleted. The claimed methods still encompass expressing SEQ ID NO: 23 and sequences similar to it in sense or antisense orientation, or both; a ribozyme; zinc finger protein; and/or an aptamer, which are all non-elected inventions.

Drawings

7. New corrected drawings are required in this application for the reasons stated in the Notice of Draftperson's Patent Drawing Review, attached to the Office action mailed January 21, 2003. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid **ABANDONMENT** of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Objections

8. Claims 47, 53, and 54 are objected to for the following reasons:

Claim 47 is objected to because of the following informalities: the recitation, -- to-- appears to be missing in line 5 after, "identical". Appropriate correction is required.

Claims 53 and 54 are objected to for being dependent on non-elected claims. As amended, claims 51 and 52 are directed to non-elected inventions. Also note: claim 51 indicates that a first expression cassette encoding a polypeptide comprising a 3'-5'

exonuclease domain, wherein the polypeptide is identical to SEQ ID NO: 24 is to be introduced a plant cell or plant. Claim 53, however, does not limit the method of claim 51, because it introduces further methods of altering the expression of the endogenous nucleotide sequence, that are not encompassed by claims 51 and 52. Therefore, even if claims 51 and 52 were examined, claims 53 and 54 would be objected to for not limiting the subject matter of a claim from which it depends.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 44, 47, and 53 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record stated in the Office action mailed January 21, 2003. Applicants traverse the rejection in the response submitted May 21, 2003. Applicants' arguments were fully considered but were not found persuasive.

Applicants argue that the claim amendments overcome the rejections (response, page 11). However, the claim amendments are not considered to overcome the rejections for the reasons set forth below.

In claims 44, 47, and 53: part f) of claim 44, part vi) of claim 47, and part (g) of claim 53, recite the recitation.

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10. Claims 25-28, 38, 39, 44, 47, 53, 54, 58, and 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 25: the meaning of the recitation, “an endogenous nucleotide sequence identical or at least 98% sequence similarity and encoding a polypeptides having 3’-5’ exonuclease activity to or SEQ ID NO: 23” is not exactly clear.

In claims 44 and 47: line 1 recites “The method for altering”. There is insufficient antecedent basis for this limitation. The article, “The” in line 1 should be replaced with --A--.

Further in claims 44 and 47: the meaning of the recitation, “ the nucleotide sequence identical or having at least 98% sequence similarity and encoding a polypeptide having 3’-5’ exonuclease activity to SEQ ID NO: 23” in part f) of claim 44 and part vi) of claim 47 is not exactly clear.

In claim 47: part vii) of the claim renders it indefinite. This part of the claim indicates that the nucleotide sequence of interest is introduced into the plant cell or plant, and that its expression is altered. However, the claim does not make clear what the expression of the nucleotide sequence of interest is being compared to, in order to determine that its expression has been altered. The nucleotide sequence has not been expressed, or even present, in the cell to this point, and it is therefore unclear how it can be said that its expression has been altered.

In claim 53: the meaning of the recitation, “the nucleotide sequence that has at least 98% sequence similarity and encodes a polypeptide having 3’-5’ exonuclease activity to SEQ ID NO: 23 or a regulatory region thereof” in part f) is not exactly clear.

Further in claim 53: the claim attempts to limit claim 52 by indicating how the expression of the endogenous nucleotide sequence mentioned in claim 51 is altered. However, claim 51 as amended indicates that the transgenic plant cell or plant comprises a first expression cassette encoding a polypeptide comprising a 3'-5' exonuclease domain, wherein the polypeptide is identical to SEQ ID NO: 24. If the transcription of the nucleotide sequence encoding the polypeptide in the first expression cassette is to lead to altered expression of the endogenous nucleotide sequence, it is not exactly clear what further alteration of expression of the endogenous nucleotide sequence is intended by the limitation of claim 53.

In claim 54: the claim is indefinite because it is dependent upon itself.

11. Claims 25-28, 38, 39, 44, 47, 53, 54, 58, and 59 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record stated in the Office action mailed January 21, 2003. Applicants traverse the rejection in the papers submitted May 21, 2003 and July 21, 2004. Applicants' arguments have been fully considered but were not found persuasive.

Applicants argue that the phrase, "substantially similar" has been deleted from the claims, and they have been amended to recite a sequence having 98% sequence similarity and encoding a protein having 3'-5' exonuclease activity (response filed May 21, 2003, page 12, 2nd full paragraph). However, the claim amendments do not sufficiently describe the sequences having 98% sequence similarity (the claims do not make it clear

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(see the indefiniteness rejections above), but it is being assumed that the similarity is to intended to be to SEQ ID NO: 23). As discussed in the Office action mailed January 21, 2003, there are many proteins that have 3'-5' exonuclease activities that do not share the same functional activities. The specification does not describe the functional activity of the protein encoded by SEQ ID NO: 23. As the specification does not completely describe the functional activity of SEQ ID NO: 24, one cannot correlate any sequences that differ from SEQ ID NO: 24 with its function.

Applicants also disagree with a statement made in the previous Office action that the specification does not teach a mutant, and point to an insertional mutant supposedly described in Example 2 (response filed May 21, 2003, page 12, 3rd full paragraph). However, Example 2 only presents a prophetic example. No mutant has actually been made. See Fiers v. Sugarno 25 USPQ 2d (CAFC 1993) at 1606, which states that “[a]n adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself”.

Applicants' response does not address the issue that no information is provided about the regulatory region of any endogenous nucleotide sequence.

12. Claims 25-28, 38, 39, 44, 47, 53, 54, 58, and 59 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record stated in the Office action mailed January 21, 2003. Applicants traverse the

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rejection in the papers submitted May 21, 2003 and July 21, 2004. Applicants' arguments have been fully considered but were not found persuasive.

Applicants again argue that the phrase, "substantially similar" has been deleted from the claims, and they have been amended to recite a sequence having 98% sequence similarity and encoding a protein having 3'-5' exonuclease activity (response filed May 21, 2003, page 13, 2nd full paragraph). However, as the full functional activity of SEQ ID NO: 24 has not been taught, it is not clear how one skilled in the art would test nucleotide sequences having 98% sequence similarity with SEQ ID NO: 23 to determine if it has the same functional activity. As discussed previously, many proteins have a 3'-5' exonuclease activity, but have different functions. Applicants also argue that one skilled in the art can produce nucleotide sequences that differ from SEQ ID NO: 23 but which encode the same protein (response filed May 21, 2003, page 13, 3rd full paragraph). The enablement of all nucleotide sequences that encode SEQ ID NO: 24 is not in question.

Regarding the claims that encompass the use of chimeric oligonucleotides, Applicants argue that the claims have been amended to delete such methods (response filed May 21, 2003, page 13, 4th full paragraph). However, claim 53 still encompasses such a method.

Regarding the issue that it is unclear that the specification does not teach the effect of reducing the expression of the endogenous nucleotide sequence on the plant, Applicants argue that Examples 5 and 9 do teach the effects (response filed May 21, 2003, page 13, 6th full paragraph). However, these examples are prophetic. The experiments discussed therein were not actually conducted. Further, Example 5 does not discuss the any effect of reducing expression of the endogenous nucleotide sequence on

the plant itself, but on a transgene. The issue concerned the global effect on the host plant. Applicants also argue that it was recently discovered that expression of certain microRNAs is reduced in the RDRD mutant, and that microRNAs have important regulatory functions (response filed May 21, 2003, paragraph bridging pages 13-14). However, this only supports the issue that reduction of the endogenous nucleotide sequence encoding a protein having 3'-5' exonuclease activity of the claims leads to adverse effects on the host plant. How is the host plant affected by the reduction of expression of the microRNAs, since they have important regulatory roles? How does one skilled in the art use such a plant?

Regarding the issue that the only manner in which the claimed method would alter the expression of the nucleotide sequence of interest is by increasing it, as expression of the endogenous nucleotide sequence of the claims is supposed to be reduced, Applicants assert that suppression of expression of SEQ ID NO: 24 results in a loss of PTGS of a nucleotide sequence of interest, and thus the claimed methods increase or "stabilize" the expression of a nucleotide sequence of interest by preventing suppression by PTGS, as compared to a parent plant that expresses the exonuclease (response filed May 21, 2003, page 14, 2nd full paragraph). However, the claimed methods encompass any type of alteration of the endogenous nucleotide sequence encoding the polypeptide having 3'-5' exonuclease activity, not just reduction of its expression, and any type of alteration of expression of the nucleotide sequence of interest, not just reduction in expression. Further, there is no mention in the claims that expression of the nucleotide sequence of interest was suppressed due to PTGS, before the expression of the endogenous nucleotide sequence was reduced.

Summary

13. Claims 51 and 52, as amended, are drawn to non-elected subject matter and are withdrawn from consideration. Claims 25-28, 38, 39, 44, 47, 53, 54, 58, and 59 remain rejected.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Contact Information

Any inquiry concerning this or earlier communications from the Examiner should be directed to Ashwin Mehta, whose telephone number is 571-272-0803. The Examiner can normally be reached from 8:00 A.M to 5:30 P.M. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Amy Nelson, can be reached at 571-272-0804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307

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for After Final communications. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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August 2, 2004



Ashwin D. Mehta, Ph.D.
Primary Examiner
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